Institution: The University of Edinburgh

Unit of Assessment: 1

Title of case study: E: Uterine artery embolisation is superior to surgery in the short term, for the treatment of symptomatic uterine fibroids

1. Summary of the impact (indicative maximum 100 words)

Impact: Health and welfare; a UK clinical trial of uterine artery embolisation (UAE), with five-year follow-up, defined the risk- and cost-benefit of UAE versus surgery.

Significance: The trial informed guidelines/recommendations internationally and changed clinical practice. Women worldwide can now make an informed choice about their treatment; economic factors have been quantitated.

Beneficiaries: Uterine fibroid patients, the NHS, healthcare providers.

Attribution: G. Murray, UoE, developed and delivered innovative trial methodology; clinical aspects led by University of Glasgow.

Reach: UK guidelines; worldwide (Australia, USA, Europe) effect on clinical practice that will impact up to 25% of women.

2. Underpinning research (indicative maximum 500 words)

Professor Gordon Murray (Professor of Medical Statistics, UoE, 1996–present) led the methodological work underpinning the first definitive trial (the REST trial) [3.1] to define the benefits and disadvantages of UAE – an intervention that had been adopted into clinical practice without evidence.

The introduction of interventional procedures into clinical practice is far less regulated than the introduction of new drugs. Surgical and other interventional procedures tend to evolve over time and are introduced into practice on the basis of being “obviously” more effective and/or less invasive than alternative procedures. Robust evaluation of the effectiveness and safety of new interventional procedures is the exception rather than the norm.

One example of an innovative procedure is uterine artery embolisation (UAE) for the treatment of symptomatic uterine fibroids. 25% of women worldwide will at some point experience these benign gynaecological tumours. UAE was introduced in 1995 and quickly became accepted as a minimally invasive alternative to hysterectomy, or, for women wishing to maintain their fertility, myomectomy. In the decade following the introduction of UAE, over 100,000 procedures were performed worldwide, without any robust evaluation of the procedure. In the UK, the National Institute for Health and Care Excellence (NICE) issued guidance in October 2004 stating that the procedure appeared to be safe for routine use and that the majority of patients gained short-term symptomatic relief. At the time, there was no robust evidence about the long-term effectiveness of the procedure.

The REST Trial (Randomised trial of Embolisation versus Surgical Treatment for Fibroids; 2000 to 2005) was a multi-centre randomised trial funded by a £280K grant from the Chief Scientist Office. The clinical aspects were led by Professor Jon Moss (University of Glasgow) and the methodological aspects (trial design, conduct, analysis, reporting and interpretation) were led by Murray. The trial recruited 157 women over 27 hospitals and was the first in this area that was both adequately powered and had long-term follow-up. The one-year follow-up data were published in the New England Journal of Medicine [3.1]. A five-year follow-up was published subsequently [3.2], as were data relating to mechanistic endpoints [3.3, 3.4].

The trial showed that UAE is indeed associated with less short-term morbidity than surgery, with, for example, a median hospital stay of one day following UAE compared with a median stay of five days following surgery. However, this must be balanced against the increased risk of minor adverse events that occur in 34% of the UAE cases (compared with 20% in the surgery group, p = 0.047), including the post-embolisation syndrome of pyrexia, pain and elevated inflammatory markers. In the UAE group, one third of women required re-intervention to control recurrent symptoms. In terms of health economics, the early savings of an average of almost £1000 per woman associated with the less invasive procedure were negated after 5 years by the need for re-intervention to control recurrent symptoms [3.2]. Thus Murray and colleagues showed that UAE and surgery had equivalent efficacy at 5 years in terms of quality of life and cost.

3. References to the research (indicative maximum of six references)

3.1 Edwards R, Moss J, Lumsden M,…Murray G; REST Investigators. Uterine-artery embolisation versus surgery for symptomatic uterine fibroids. N Engl J Med. 2007;356:360–70. DOI: 10.1056/NEJMoa062003. *[Cited 211 times as of 12-Aug 2013.]*

3.2 Moss J, Cooper K, Khaund A,…Murray G, et al. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG. 2011;118:936–44. DOI: 10.1111/j.1471-0528.2011.02952.x.

3.3 Rashid S, Khaund A, Murray L,…Murray G, Lumsden M. The effects of uterine artery embolisation and surgical treatment on ovarian function in women with uterine fibroids. BJOG. 2010;117:985–9. DOI: 10.1111/j.1471-0528.2010.02579.x.

3.4 Ananthakrishnan G, Murray L, Ritchie M, Murray G, et al. Randomized comparison of uterine artery embolization (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST Trial): subanalysis of 5-year MRI findings. Cardiovasc Intervent Radiol. 2013;36:676–81. DOI: 10.1007/s00270-012-0485-y.

4. Details of the impact (indicative maximum 750 words)

Approximately 50% of hysterectomies performed worldwide are for the treatment of symptomatic uterine fibroids (12,000 per year in the UK). Fibroids thus constitute a major public health problem and it was crucial to know whether UAE is a useful alternative. Murray's work has clarified that UAE is superior to surgery in the short term.

Impact on public policy

The REST trial has informed key clinical guidelines. The 2010 NICE guidance on UAE for fibroids [5.1] was informed by Murray and colleagues' publication [3.1] together with a pre-publication version of the follow-up paper [3.2]. The fact that NICE sought this pre-publication version reflects the lack of robust long-term evidence prior to the REST trial being conducted. The REST results also formed a key part of the evidence base for the 2009 report by a joint working party of the Royal College of Obstetricians and Gynaecologists and the Royal College of Radiologists on the use of UAE in the management of fibroids [5.2]. The REST study is also cited in NICE guidelines on heavy menstrual bleeding [5.3], which endorse the use of UAE for treatment of fibroids.

Internationally, REST is cited by the American College of Radiology Appropriateness Criteria® Expert Panel on Interventional Radiology [5.4] and in a review published in the Australian and New Zealand Journal of Obstetrics and Gynaecology [5.5], both of which endorse the use of UAE, based on the REST data.

The relevant Cochrane systematic review was updated in 2012 [5.6]. There are still only six randomised trials published in the area, only two of which (including REST) report follow-up data to 5 years. Notably, REST has the greatest number of UAE procedures to be evaluated within any single randomised trial.

In addition, the primary publication [3.1] has affected professional standards for reporting trial results, with the paper being flagged in the British Medical Journal [5.7] as a model for good

reporting of patient flow through a trial.

Impact on clinical practice
Although the numbers of UAE procedures are not readily available, a 2011 survey by the Medical Technology Group [5.8] showed that 90% of primary care trusts in England now routinely commission UAE, with UAE accounting for 10% of all in-patient treatments for women with fibroids. Across Europe, a 2009 survey of members of the Cardiovascular and Interventional Radiological society of Europe [5.9] showed widespread access to UAE, with the UK containing the greatest number of providing centres. The REST trial was again cited in this survey as providing clinical rationale for the procedure.

Impact on health and wellfare
Women considering UAE rather than hysterectomy as a treatment for their symptomatic fibroids are now able to make an informed choice comparing the immediate benefits (including faster recovery time) of the less-invasive UAE against the greater 5-year risk (32% with UAE compared with 4% with surgery) of the need for subsequent re-intervention to control emergent symptoms.

Impact on the economy
The Royal College of Obstetricians and Gynaecologists working party report [5.2] highlights the finding that although UAE is cost-effective relative to surgery when evaluated at 12-months follow-up, the economic benefit in favour of UAE diminishes over time with the increased need for re-interventions, and is negated after five years.

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1 NICE guidelines (2010) Uterine artery embolisation for fibroids. Interventional procedures guidance IPG367. http://guidance.nice.org.uk/IPG367.

5.2 Royal College of Obstetricians and Gynaecologists and the Royal College of Radiologists (2009). Clinical recommendations on the use of uterine artery embolisation in the management of fibroids. Second edition. http://www.rcog.org.uk/files/rcog-corp/uploaded-files/WPRUterineArteryEmbolisation2009.pdf.

5.3 NICE guidelines (2007). Heavy menstrual bleeding. Clinical guideline no. 44. http://www.nice.org.uk/cg44. *NB. [This remains the current guideline for the period 2008–13.]*

5.4 USA recommendations. Burke C, Funaki B, Ray C Jr, et al. ACR Appropriateness Criteria® on treatment of uterine leiomyomas. J Am Coll Radiol. 2011;8:228–34. DOI: 10.1016/j.jacr.2010.12.020.

5.5 Australasia recommendations. Hickey M, Hammond I. What is the place of uterine artery embolisation in the management of symptomatic uterine fibroids? Aust N Z J Obstet Gynaecol. 2008;48:360–8. DOI: 10.1111/j.1479-828X.2008.00886.x.

5.6 Gupta JK, Sinha A, Lumsden M, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syste Rev. 2012; 5:CD005073. DOI: 10.1002/14651858.CD005073.pub3.

5.7 Pocock S, Travison T, Wruck L. How to interpret figures in reports of clinical trials. BMJ. 2008;336:1166–9. DOI: 10.1136/bmj.39561.548924.94.

5.8 Medical Technology Group (2011). “Your first choice – the provision of and access to UFE”. http://www.mtg.org.uk/index.php/policy-initiatives/mtg-campaigns/8-a-review-of-the-provision-of-and-access-to-uterine-arteryfibroid-embolisation-a-treatment-for-fibroids-for-women-in-england.

5.9 Voogt M, Arntz M, Lohle P, Mali W, Lampmann LE. Uterine fibroid embolisation for symptomatic uterine fibroids: a survey of clinical practice in Europe. Cardiovasc Intervent Radiol. 2011;34:765–73. DOI: 10.1007/s00270-010-9978-8.